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EXAMINER

SANG, HONG

ART UNIT	PAPER NUMBER
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1643

DATE MAILED: 04/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/801,517	QI, XIAOYANG	
	Examiner	Art Unit	
	Hong Sang	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 March 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-49 is/are pending in the application.
- 4a) Of the above claim(s) 9-43 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8 and 44-49 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 16 March 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>6/18/04 & 10/8/04</u> . | 6) <input checked="" type="checkbox"/> Other: <u>Exhibits A-D</u> . |

DETAILED ACTION

RE: QI

1. Applicant's election with traverse of Group I (claims 1-8 and 44-49) and SEQ ID NO.2 in the reply filed on 3/1/2006 is acknowledged. The traversal is on the ground(s) that restriction requirement between SEQ ID NOS.1 and 2 is improper because the sequences represented by the two sequences of SEQ ID NOS. 1 and 2 represent the protein and pro-protein of the very same protein. The full search of the art for one sequence would necessarily include the second sequence. This is found persuasive. Accordingly, SEQ ID NOS.1 and 2 are examined together.

The requirement except the one set forth above is still deemed proper and is therefore made FINAL.

2. Claims 1-49 are pending. Claims 6, 17 and 29 are amended. Claims 9-43 are withdrawn from further consideration as being drawn to non-elected inventions.

3. The information disclosure statements (IDS) filed on 6/18/2004 and 10/8/2004 have been considered. Signed copies are attached hereto.

4. Claims 1-8 and 44-49 are under examination.

Specification

5. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code see page 13, line 18, for example. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code found throughout the specification. See MPEP § 608.01.

Claim Objections

6. Claim 5 is objected to because it depends on itself. Correction is required.

Claim Rejections - 35 USC § 112, 1st paragraph

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants recite the term "an inner leaflet component", and "a prosaposin-related polypeptide comprising an amino acid sequence having 80% identical to SEQ ID NO.1 or 2. The specification teaches that the "inner leaflet component" refers to any molecule or structural analog thereof naturally occurring in the inner leaflet of a plasma membrane of a cell, particularly an animal cell, more particularly a mammalian cell (see page 4, paragraph [0012], lines 3-6). The written description in this instant case only sets forth anionic phospholipid, particularly phosphatidylserine, SEQ ID NO.1 and SEQ ID NO.2. Therefore the written description is not commensurate in scope with the claims which read on any and all inner leaflet component, and any and all sequences that are at least 80% identical to SEQ ID NO.1 or 2. There is a lack of a written

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description regarding which amino acids within the full-length amino acid sequence of SEQ ID NO.1 or 2 that can be changed by deletion, addition, substitution or combination thereof such that the resulting sequence that is at least 80% identical to SEQ ID NO.1 or 2 still has same function as SEQ ID NO.1 or 2. The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

Applicant does not appear to have reduced to practice all inner leaflet components, and all sequences that are at least 80% identical to SEQ ID NO.1 or 2. The inner leaflet component includes lipid, protein, and carbohydrates. The written description only sets forth anionic phospholipids, particularly phosphatidylserine. Moreover, applicant fails to provide sufficient descriptive information such as definitive structural or functional features that are common to the genus of the sequences that are at least 80% identical to SEQ ID NO.1 or 2, the genus of the of inner leaflet component, and structural analog of phosphatidylserine. Because the genus of molecules encompassed by the term inner leaflet component, and a sequence that is at least 80%

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identical to SEQ ID NO.1 or 2 is extensive and the artisan cannot envision the detailed structure of the encompassed molecules, therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Thus one of skill in the art would not be able to recognize that applicant was in possession of the invention as now claimed.

Consequently, Applicant was not in possession of the instant claimed invention. See Regents of the University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). Adequate written description of genetic material "requires a precise definition, such as by structure, formula, chemical name, or physical properties,' not a mere wish or plan for obtaining the claimed chemical invention." Id. 43 USPQ2d at 1404 (quoting Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606). The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter of the claim. Id. 43 USPQ2d at 1406. A description of what the genetic material does, rather than of what it is, does not suffice. Id.

Therefore, anionic phospholipids, SEQ ID NOS. 1 and 2 but not the full breadth of "inner leaflet component", and "sequences that are at least 80% identical to SEQ ID NO.1 or 2 meet the written description provision of 35 U.S.C. § 112 first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is invited to point to clear support or specific examples of the claimed invention in the specification as-filed.

Claim Rejections - 35 USC § 112, 1st paragraph

9. Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an agent comprising an anionic phospholipid, particularly phosphatidylserine and a prosaposin polypeptide of SEQ ID NO.1 or SEQ ID NO.2, does not reasonably provide enablement for an agent comprising any and all inner leaflet component, and any and all prosaposin-related polypeptide of an amino acid sequence that is at least 80% identical to SEQ ID NO.1 or 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The claims are drawn to an agent comprising an inner leaflet component and a prosaposin-related polypeptide, wherein said polypeptide has an amino acid sequence that is SEQ ID NO.1, SEQ ID NO.2, or at least 80% identical to SEQ ID NO.1 or 2.

The invention is in a class of invention, which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." *Mycogen Plant Sci., Inc. v. Monsanto Co.*, 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The breadth of the claims

The "inner leaflet component" recited in the claims encompasses any molecule or structural analog thereof naturally occurring in the inner leaflet of a plasma membrane of a cell, particularly an animal cell, more particularly a mammalian cell (see page 4, paragraph [0012], lines 3-6). Therefore, the "inner leaflet component" includes lipid, protein and carbohydrate.

The prosaposin-related polypeptide comprises any and all homologs and fragments of SEQ ID NO.1 or 2 that are at least 80% identical to SEQ ID NO.1 and 2.

Quantity of experimentation

The quantity of experimentation in this area is extremely large since there is significant variability in the structure and effects of inner leaflet component, and prosaposin polypeptide fragments or homologues that are at least 80% identical to SEQ ID NO.1 or 2. Moreover, it would require significant study to determine which of the prosaposin fragments or homologues of SEQ ID NO.1 or 2 that are at least 80% identical are in fact capable of interact with cell plasma membrane. The identification and characterization of each of these fragments or homologues would be inventive, unpredictable, and difficult in itself, requiring years of inventive effort with no guarantee

of success in doing so.

One cannot extrapolate the teachings of the specification to the scope of the claims because the claims are broadly drawn to an agent comprising any inner leaflet component and any prosaposin fragment, or homologues that are at least 80% identical to SEQ ID NO.1 or 2 with or without the biological properties representative of what is claimed, and applicant has not enabled all of these types of modified polypeptides because it has not been shown that these modified proteins are capable of functioning as that which is being disclosed.

Although the claims recite the function limitation "wherein said polypeptide retains plasma-membrane affinity", one skilled in the art still would not know how to identify these sequences among those that are at least 80% identical to SEQ ID NO.1 or 2 without the guidance of required definitive structural.

The state of the prior art and the predictability or lack thereof in the art:

Protein chemistry is probably one of the most unpredictable areas of biotechnology. It is known in the art that the relationship between the amino acid sequence of a protein (polypeptide) and its tertiary structure (i.e. its binding activity) are not well understood and are not predictable (see Ngo et al., in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz, et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495). There is no recognition in the art that sequence with identity predicts biological function. It is known in the art that even single amino acid changes or differences in a protein's amino acid sequence can have dramatic effects on the

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protein's function. For example, conservative replacement of a single "lysine" residue at position 118 of acidic fibroblast growth factor by "glutamic acid" led to the substantial loss of heparin binding, receptor binding and biological activity of the protein (Burgess et al., J of Cell Bio. 111:2129-2138, 1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (Lazar et al. Molecular and Cellular Biology 8:1247-1252, 1988). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein. Furthermore, the specification fails to teach what deletions, truncations, substitutions and mutations of the disclosed sequence can be tolerated that will allow the protein to function as claimed. While it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with reasonable expectation of success are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or no substitutions. Residues that are directly involved in protein functions such as binding will certainly be among the most conserved (Bowie et al. Science, 247:1306-1310, 1990, p. 1306, col.2).

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth, and it cannot be predicted from the disclosure how to use any and all sequences that are at least 80% identical to SEQ ID NO. 1 or 2. Therefore, in view of

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the lack of predictability of the prior art, the breadth of the claims and the absence of working examples, it would require undue experimentation for one skilled in the art to practice the invention as claimed.

Working examples:

The specification teaches purification of recombinant saposin C (see Example 1) and bath sonication of saposin C and dioleoylphosphatidylserine (DOPS) (see Example 2). The specification teaches *ex vivo* analysis of effects of saposin C-DOPS on cells and *in vivo* analysis of saposin C-DOPS on tumor volume (see examples 4-8).

The specification does not teach how to make and use any other prosaposin-related polypeptide, and any other inner leaflet component.

Guidance in the specification

While one of ordinary skill in the art can theoretically produce all of these prosaposin-related polypeptides with art known techniques such as site-directed mutagenesis it would still be burdensome to one of ordinary skill in the art to produce all of these different combinations and thereafter determine their activity. It is art known that certain residues are shown to be particularly important to the biological or structural properties of a protein or peptide, e.g., residues in active sites and such residues may not be generally be exchanged. Skolnick et al teach that sequence-based methods for function prediction are inadequate and knowing a protein's structure does not tell one its function (Skolnick, et al. Trends in Biotech. 18, 34-39, 2000, see abstract, in particular).

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Given the unlimited number of sequences that are at least 80% identical to SEQ ID NO.1 or 2, there is insufficient working example demonstrating that the undisclosed polypeptides can still function as SEQ ID NO.1 or 2. Moreover, it is not clear what criteria would be used in deciding which amino acids and how many of them would and could be substituted in the wild type polypeptides and what amino acid residues would represent SEQ ID NO.1 or 2. Without such guidance, the changes which can be made in the protein structure and still maintain activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 and *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of *Ex parte Aggarwal*, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

Level of skill in the art

The level of the skill in the art is deemed to be high

Conclusion:

Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of the art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of a working example of any other inner leaflet component and any prosaposin-related

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polypeptide and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-8 and 44-49 are rejected under 35 U.S.C. 102(b) as being anticipated by Morimoto et al. (J. Bio. Chem., 1990, 265(4): 1933-1937), and as evidenced by Morimoto et al. (Proc. Natl. Acad. Sci. U.S.A., 1989: 86: 3389-3393).

Claims are drawn to an agent comprising an inner leaflet component and a prosaposin-related polypeptide, wherein said polypeptide has an amino acid sequence of SEQ ID NO.1, 2 or at least 80% identical to SEQ ID NO.1 or 2, said inner leaflet component is phosphatidylserine, dioleoylphosphatidylserine, the molar ratio of said polypeptide to said inner leaflet component is in the range from about 1:1 to about 1:50, from about 1:1 to about 1:10, further comprising a pharmaceutically acceptable carrier, said agent promotes cell death in hyper-proliferating cells, said hyper-proliferating cells are selected from the group consisting of tumor cells and cancer cells.

Claims are also drawn to an anti-tumor agent comprising a polypeptide having the amino acid sequence set forth in SEQ ID NO. 2 and dioleoylphosphatidylserine,

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wherein the mass ratio of polypeptide to dioleoylphosphatidylserine is approximately 5:1, approximately 15:7, in the range from about 15: 1 to about 3:10, comprising approximately 10 μ M polypeptide and approximately 30 μ M dioleoylphosphatidylserine, comprising approximately 10 μ M polypeptide and approximately 70 μ M dioleoylphosphatidylserine.

Morimoto et al. teach an agent (an assay mixture) comprising saposin C, dioleoylphosphatidylserine and glucosylceramidase (see page 1933, under materials, and page 1934, 1st paragraph). The concentration of saposin C is from 0-20 μ M (see Fig.2), and of phosphatidylserine is from 0-200 μ M (see Fig. 3). The mass ratio of saposin C (7 μ g or 10 μ g) to dioleoylphosphatidylserine (0.65 nmol is 0.5 μ g) is about 13:1 or 20:1, and the molar ratio of saposin C to dioleoylphosphatidylserine is about 1:1-1:10 (see page 1934, left column, under Results, lines 15-16, Fig. 1, column 7). The mass ratio of saposin C to dioleoylphosphatidylserine can also be about 1:1 (see Fig.2 and Fig.3). The sequences of the saposin C and A of Morimoto et al. are 100% identical to the instant SEQ ID NO.1 or 2 (see page 1933, right column, under materials, lines 1-2), as evidence by Morimoto et al. (PNAS USA, 1989, 36:3389-3393) and the sequence alignment (see Exhibit A). Morimoto et al. teach the pharmaceutical carrier e.g. acetate buffer (see page 1934, left column, line 6).

Although Morimoto et al. do not teach that the agent comprising saposin C and dioleoylphosphatidylserine have anti-tumor activity or promotes death in cancer cells, the claims are drawn to a product *per se* and inherently, such an agent would have anti-tumor activity. Thus, the claimed agent appears to be the same as the prior art. The

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office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See *In re Best* 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Moreover, since the claims use the term "comprising" which is open, and the term "about", Morimoto et al. teach all the claim limitations.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. Claims 1-8 and 44-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vaccaro et al. (FEBS 1993, 336(1): 159-162) in view of the teachings of O'brien et al. (WO9503821A1).

Claims' limitations are set forth above (see paragraph 11 above)

Vaccaro et al. teach an agent (an assay mixture) comprising saposin C, dioleoylphosphatidylserine and glucosylceramidase (see page 160 paragraph 2.5, and page 159, under materials, line 5). The concentration of saposin C is from 0-25 µg/ml

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(see Fig.1). The amount of phosphatidylserine is from 0-80 μ g (see Fig. 1, 2 and Table 1). The mass ratio of saposin C to dioleoylphosphatidylserine is about 1:3 or 5:1 (see Table 1 and Fig.2). The molar ratio of saposin C to dioleoylphosphatidylserine is about 1:1-1:10 (after calculation). Vaccaro et al. teach the pharmaceutical carrier e.g. acetate buffer (see page 160, paragraph 2.5)

Vaccaro et al. do not teach that the sequence of Saposin C is SEQ ID NO.2. However, these deficiencies are made up for in the teachings of O'brien et al.

O'brien et al. teach that the sequence of saposin C (see page 32). The sequence of saposin C is 100% identical the instant SEQ ID NO.2 (see sequence alignment Exhibit B).

It would have been prima fascia obvious to one skilled in the art at the time the invention was made to have used saposin C of SEQ ID NO.2 to make the agent of Vaccaro in view of the teachings of O'brien. One would have been motivated to use the saposin C of SEQ ID NO.2 to make the agent of Vaccaro because SEQ ID NO. 2 is saposin C and O'brien teaches how to make SEQ ID NO.2. One would have had an expectation of success at the time the invention was made to use saposin C of SEQ ID NO.2 to make the agent of Vaccaro because Vaccaro et al. teach the agent comprising saposin C and phosphatidylserine and O'brien teach the saposin C of SEQ ID NO.2.

Although Vaccaro et al. do not teach that the agent comprising saposin C and dioleoylphosphatidylserine have anti-tumor activity or promotes death in cancer cells, the claims are drawn to a product *per se* and inherently, such an agent would have anti-tumor activity. Thus, the claimed agent appears to be the same as the prior art. The

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office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See *In re Best* 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Moreover, since the claims use the term "comprising" which is open, and the term "about", Vaccaro et al. and O'brien et al. teach all the claim limitations.

Double Patenting

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

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15. Claims 1-3 and 44-47 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 16, 17, 21 and 22 of U.S. Patent No. 6,872,406 in view of Vaccaro et al. (FEBS Lett. 1994, 349: 181-186, IDS). Although the conflicting claims are not identical, they are not patentably distinct from each other.

The limitations of claims 1-3 and 44-47 are set forth above (see paragraph 11 above).

Claims 16, 17, 21 and 22 of U.S. Patent No. 6,872,406 are drawn to a therapeutic phospholipid composition comprising: a) an anionic phospholipids, b) a safe and effective amount of the pharmaceutical agent contained within the aqueous interior of the phospholipids; and c) a fusogenic protein or polypeptide derived from prosaposin; in a pharmaceutically acceptable carrier, wherein the fusogenic protein or polypeptide is present in a sufficient concentration to deliver the pharmaceutical agent through a biological membrane and the fusogenic protein or polypeptide is associated with the phospholipids through an electrostatic and hydrophobic interaction. The claims are further limited wherein the concentration of anionic phospholipids is in at least 10-fold excess, by weight, to that of the fusogenic protein or polypeptide, the fusogenic protein or polypeptide is selected from the group consisting of saposin A, and saposin C.

The sequence of Saposin C of the US Patent No. 6,872,406 is identical to the instant SEQ ID NO. 2 (see Fig. 4 of the patent, and the sequence alignment Exhibit C). The instant claims recite the term "structural analog of phosphatidylserine" and the instant specification defines the structural analog of phosphatidylserine as an anionic

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phospholipid. Because the instant claims using “comprising” which is an open language, the claims 16, 17, 21 and 22 of US patent No. 6,872,406 anticipate the instant claims 1 and 2.

Claims 16, 17, 21 and 22 of U.S. Patent No. 6,872,406 do not teach phosphatidylserine or dioleoylphosphatidylserine. However, these deficiencies are made up for in the teachings of Vaccaro et al.

Vaccaro et al. teach that saposin C induces pH-dependent destabilization and fusion of phosphatidylserine (particularly dioleoylphosphatidylserine)-containing vesicles (see abstract, and page 182 under materials).

It would have been *prima facie* obvious to one skilled in the art at the time the invention was made to make a therapeutic phospholipid composition comprising phosphatidylserine, particularly dioleoylphosphatidylserine in view of the teachings of claims 16, 17, 21 and 22 of U.S. Patent No. 6,872,406 and Vaccaro. One would have been motivated to use phosphatidylserine, particularly dioleoylphosphatidylserine to make a therapeutic phospholipid composition because Vaccaro teach that saposin C induces destabilization and fusion of phosphatidylserine, particularly dioleoylphosphatidylserine. One would have had an expectation of success at the time the invention was made to use dioleoylphosphatidylserine, particularly dioleoylphosphatidylserine to make the a therapeutic phospholipid composition because claims 16, 17, 21 and 22 of U.S. Patent No. 6,872,406 teach how to make and use a therapeutic composition comprising an anionic phospholipid.

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16. Claims 1-3 and 44-47 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16, 17, 21 and 22 of copending Application No. 10/967,921 in view of Vaccaro et al. (FEBS Lett. 1994, 349: 181-186, IDS). Although the conflicting claims are not identical, they are not patentably distinct from each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The limitations of claims 1-3 and 44-47 are set forth above (see paragraph 11 above).

Claims 16, 17, 21 and 22 of copending Application No. 10/967,921 are drawn to a therapeutic phospholipid composition comprising: a) an anionic phospholipids, b) a safe and effective amount of the pharmaceutical agent contained within the aqueous interior of the phospholipids; and c) a fusogenic protein or polypeptide derived from prosaposin; in a pharmaceutically acceptable carrier, wherein the fusogenic protein or polypeptide is present in a sufficient concentration to deliver the pharmaceutical agent through a biological membrane and the fusogenic protein or polypeptide is associated with the phospholipids through an electrostatic and hydrophobic interaction. The claims are further limited wherein the concentration of anionic phospholipids is in at least 10-fold excess, by weight, to that of the fusogenic protein or polypeptide, the fusogenic protein or polypeptide is selected from the group consisting of saposin A, and saposin C.

The sequence of saposin C of the copending Application No. 10/967,921 is identical to the instant SEQ ID NO. 2 (see Fig. 4 of the patent, and the sequence alignment Exhibit D). The instant claims recite the term “structural analog of phosphatidylserine” and the instant specification defines the structural analog of phosphatidylserine as an anionic phospholipid. Because the instant claims using “comprising” which is an open language, the claims 16, 17, 21 and 22 of the copending Application No. 10/967,921 anticipate the instant claims 1 and 2.

Claims 16, 17, 21 and 22 of copending Application No. 10/967,921 do not teach phosphatidylserine or dioleoylphosphatidylserine. However, these deficiencies are made up for in the teachings of Vaccaro et al.

Vaccaro et al. teach that saposin C induces pH-dependent destabilization and fusion of phosphatidylserine (particularly dioleoylphosphatidylserine)-containing vesicles (see abstract, and page 182 under materials).

It would have been *prima facie* obvious to one skilled in the art at the time the invention was made to make a therapeutic phospholipid composition comprising phosphatidylserine, particularly dioleoylphosphatidylserine in view of the teachings of claims 16, 17, 21 and 22 of copending Application No. 10/967,921 and Vaccaro. One would have been motivated to use phosphatidylserine, particularly dioleoylphosphatidylserine to make a therapeutic phospholipid composition because Vaccaro teach that saposin C induces destabilization and fusion of phosphatidylserine, particularly dioleoylphosphatidylserine. One would have had an expectation of success at the time the invention was made to use phosphatidylserine, particularly

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dioleoylphosphatidylserine to make the a therapeutic phospholipid composition because claims 16, 17, 21 and 22 of copending Application No. 10/967,921 teach how to make and use a therapeutic composition comprising an anionic phospholipid.

Conclusion

17. No claims are allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hong Sang whose telephone number is (571) 272 8145. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hong Sang
Art Unit 1643
Mar. 10, 2006



LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER

US-10-801-517-2.rup

Wed Jan 18 11:58:43 2006

RT same genetic locus."; (1988).
RL Science 241:1098-1101(1988).
RN [6]
RP NUCLEOTIDE SEQUENCE OF 14-524.
RX MEDLINE=92307663; PubMed=1612590;
RA Korman E.G., Scheinker V., Grabowski G.A.;
RT "Structure and evolution of the human prosaposin chromosomal gene.";
RL Genomics 13:312-318(1992).
RN [7]
RP PROTEIN SEQUENCE OF 17-24; 165-172; 180-189 AND 298-302.
RX MEDLINE=93311991; PubMed=8323276; DOI=10.1006/abbi.1993.1328;
RA Hiraiwa M., O'Brien J.S., Kishimoto Y., Galdzicka M., Fluharty A.L.,
RX Gims E.I., Martin B.M.;
RT "Isolation, characterization, and proteolysis of human prosaposin, the
RT precursor of saposins (sphingolipid activator proteins).";
RL Arch. Biochem. Biophys. 304:110-116(1993).
RN [8]
RP PROTEIN SEQUENCE OF 17-26.
RX TISSUE=Milk;
RC MEDLINE=92068206; PubMed=1958198;
RA Kondoh K., Hineno T., Sano A., Kakimoto Y.;
RT "Isolation and characterization of prosaposin from human milk.";
RL Biochem. Biophys. Res. Commun. 181:286-292(1991).
RN [9]
RP NUCLEOTIDE SEQUENCE OF 59-125 AND 304-513.
RX TISSUE=Brain;
RC MEDLINE=91192146; PubMed=2013321; DOI=10.1016/0014-5793(91)80308-P;
RA Holtschmidt H., Sandhoff K., Fuerst W., Kwon H.Y., Schnabel D.,
RA Suzuki K.;
RT "The organization of the gene for the human cerebroside sulfate
RT activator protein.";
RL FEBS Lett. 280:267-270(1991).
RN [10]
RP PARTIAL PROTEIN SEQUENCE OF 60-142.
RX MEDLINE=89240739; PubMed=2717620;
RA Morimoto S., Martin B.M., Yamamoto Y., Kretz K.A., O'Brien J.S.,
RA Kishimoto Y.;
RT "Saposin A: second cerebroside activator protein.";
RL Proc. Natl. Acad. Sci. U.S.A. 86:3389-3393(1989).
RN [11]
RP PROTEIN SEQUENCE OF 62-84 AND 410-431.
RX MEDLINE=93380576; PubMed=8370464; DOI=10.1016/0014-5793(93)80908-D;
RA Tynnela J., Palmer D.N., Baumann M., Haltia M.;
RT "Storage of saposins A and D in infantile neuronal ceroid-
RT lipofuscinosis.";
RL FEBS Lett. 330:8-12(1993).
RN [12]
RP NUCLEOTIDE SEQUENCE OF 164-524.
RX MEDLINE=88068647; PubMed=2825202;
RA Dewji N.N., Wenger D.A., O'Brien J.S.;
RT "Nucleotide sequence of cloned cDNA for human sphingolipid activator
RT protein 1 precursor.";
RL Proc. Natl. Acad. Sci. U.S.A. 84:8652-8656(1987).
RN [13]
RP NUCLEOTIDE SEQUENCE OF 195-263.
RX MEDLINE=86130593; PubMed=2868718;
RA Dewji N.N., Wenger D.A., Fujibayashi S., Donoviel M., Esch P.,
RA Hall F., O'Brien J.S.;
RT "Molecular cloning of the sphingolipid activator protein-1 (SAP-1),
RT the sulfate sulfate activator protein.";
RL Biochem. Biophys. Res. Commun. 134:989-994(1986).
RN [14]
RP PROTEIN SEQUENCE OF 195-274.
RX MEDLINE=9207118; PubMed=3242555;
RA Kleinschmidt T., Christomanou H., Braunitzer G.;
RT "Complete amino-acid sequence of the naturally occurring A2 activator
RT protein for enzymic sphingomyelin degradation: identity to the
RT sulfate activator protein (SAP-1).";
RL Biol. Chem. Hoppe-Seyler 369:1361-1365(1988).
RN [15]
RP PROTEIN SEQUENCE OF 195-274.
RX TISSUE=Kidney;
RC MEDLINE=91006165; PubMed=2209618;
RX

RESULT 2
ID SAP HUMAN STANDARD; PRT: 524 AA.
AC P07602; P07292; P15793; P78538; P78541; P78546; P78547; P78558;
AC O61B06; Q92739; Q92740; Q92741; Q92742;
DT 01-APR-1988 (Rel. 07, Created)
DT 01-APR-1990 (Rel. 14, Last sequence update)
DT 13-SEP-2005 (Rel. 48, Last annotation update)
DE Proactivator polypeptide precursor [Contains: Saposin A (Protein A);
DE Saposin B-Val; Saposin B (Sphingolipid activator protein 1) (SAP-1)
DE (Cerebroside sulfate activator) (CSA) (Dispersin) (Sulfatide/GM1
DE activator); Saposin C (Co-beta-glucosidase) (AI activator)
DE (Glucosylceramidase activator) (Sphingolipid activator protein 2)
DE (SAP-2); Saposin D (Protein C) (Component C)].
GN Name=PSAP;
OS Homo sapiens (Human).
OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini; Hominidae;
OC Homo.
OX NCBI_TaxID=9606;
RN NUCLEOTIDE SEQUENCE [MRNA].
RP TISSUE=Liver;
RC MEDLINE=90129043; PubMed=2515150;
RX Korman E.G., Grabowski G.A.;
RA "Molecular cloning of a human co-beta-glucosidase cDNA: evidence that
RT four sphingolipid hydrolase activator proteins are encoded by single
RT genes in humans and rats.";
RL Genomics 5:486-492(1989).
RN [2]
RP NUCLEOTIDE SEQUENCE [MRNA].
RX MEDLINE=89255151; PubMed=2498298;
RA Nakano T., Sandhoff K., Stuemper J., Christomanou H., Suzuki K.;
RT "Structure of full-length cDNA coding for sulfate activator, a Co-
RT beta-glucosidase and two other homologous proteins: two alternate
RT forms of the sulfate activator.";
RL J. Biochem. 105:152-154(1989).
RN [3]
RP NUCLEOTIDE SEQUENCE [LARGE SCALE MRNA].
RX Ebert L., Schick M., Neubert P., Schatten R., Henze S., Korn B.;
RT "Cloning of human full open reading frames in Gateway(TM) system entry
RT vector (pDONR201).";
RL Submitted (JUN-2004) to the EMBL/GenBank/DBJ databases.
RN [4]
RP NUCLEOTIDE SEQUENCE [LARGE SCALE MRNA] (ISOFORM SAP-WU-0).
RC TISSUE=Brain, Eye, and Skin;
RX MEDLINE=22388257; PubMed=12477932; DOI=10.1073/pnas.242603899;
RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,
RA Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,
RA Altschul S.F., Zeeberg B., Buettow K.H., Schaefer C.F., Bhat N.K.,
RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Haie P.,
RA Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,
RA Scapleton M., Soares M.B., Bonaldo M.F., Casavant T.D., Scheetz T.B.,
RA Brownstein M.J., Udell T.B., Toshiyuki S., Carninci P., Prange C.,
RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullaly S.J.,
RA Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,
RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,
RA Vallalou D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,
RA Fahney J., Helton E., Kettelman M., Madan A., Rodriguez S., Sanchez A.,
RA Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,
RA Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,
RA Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,
RA Butterfield Y.S.N., Krzyzinski M.I., Skalska U., Smallus D.B.,
RA Schnerch A., Schein J.B., Jones S.J.M., Marra M.A.;
RT "Generation and initial analysis of more than 15,000 full-length human
RT and mouse cDNA sequences.";
RL Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).
RN [5]
RP NUCLEOTIDE SEQUENCE OF 14-524.
RX MEDLINE=98321660; PubMed=2842863;
RA O'Brien J.S., Kretz K.A., Dewji N., Wenger D.A., Esch P.,
RA Fluharty A.L.;
RT "Cloning of two sphingolipid activator proteins (SAP-1 and SAP-2) by

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RA Pust W., Schubert J., Machleidt W., Meyer H.E., Sandhoff K.;
RT "The complete amino-acid sequences of human ganglioside GM2 activator
RL protein and cerebroside sulfate activator protein.";
RN Eur. J. Biochem. 192:709-714 (1990).
RX MEDLINE=88163077; PubMed=3442600;
RA Kleinschmidt T., Christomanou H., Braunitzer G.;
RT "Complete amino-acid sequence and carbohydrate content of the
RL naturally occurring glucosylceramide activator protein (A1 activator)
RN absent from a new human Gaucher disease variant.";
RX Biol. Chem. Hoppe-Seyler 368:1571-1578 (1987).
RA PARTIAL PROTEIN SEQUENCE OF 311-390.
RX MEDLINE=88163077; PubMed=3442600;
RA Kleinschmidt T., Christomanou H., Braunitzer G.;
RT "Complete amino-acid sequence and carbohydrate content of the
RL naturally occurring glucosylceramide activator protein (A1 activator)
RN absent from a new human Gaucher disease variant.";
RX Biol. Chem. Hoppe-Seyler 368:1571-1578 (1987).
RA PARTIAL PROTEIN SEQUENCE OF 405-484.
RX MEDLINE=89025876; PubMed=2845979;
RA Morimoto S., Martin B.M., Kishimoto Y., O'Brien J.S.;
RT "Saposin D: a sphingomyelinase activator.";
RL Biochem. Biophys. Res. Commun. 156:403-410 (1988).
RA PROTEIN SEQUENCE OF 407-484.
RX MEDLINE=89025876; PubMed=2845979;
RA Furst W., Machleidt W., Sandhoff K.;
RT "The precursor of sulfatide activator protein is processed to three
RL different proteins.";
RX Biol. Chem. Hoppe-Seyler 369:317-328 (1988).
RA PARTIAL PROTEIN SEQUENCE (SAPOSIN B), AND STRUCTURE OF CARBOHYDRATES.
RX MEDLINE=20032116; PubMed=10562467; DOI=10.1006/mgme.1999.2900;
RA Fluharty A.L., Lombardo C., Louis A., Stevens R.L., Whitelegge J.P.,
RT Waring A.J., To T., Fluharty C.B., Faull K.P.;
RL "Preparation of the cerebroside sulfate activator (CSact or saposin B)
RX from human urine.";
RA Mol. Genet. Metab. 68:391-403 (1999).
RA DISULFIDE BONDS OF SAPOSINS B AND C, AND MASS SPECTROMETRY.
RX MEDLINE=95247790; PubMed=7730378; DOI=10.1074/jbc.270.17.9953;
RA Vaccaro A.M., Salvio R., Barca A., Tatti M., Ciaffoni P., Maras B.,
RT Siciliano R., Zappacosta F., Amoresano A., Pucci P.;
RL "Structural analysis of saposin C and B. Complete localization of
RX disulfide bridges.";
RA J. Biol. Chem. 270:9953-9960 (1995).
RA STRUCTURE OF CARBOHYDRATE ON ASN-215.
RX MEDLINE=21110404; PubMed=11180632;
RA Faull K.P., Johnson J., Kim M.J., To T., Whitelegge J.P.,
RT Stevens R.L., Fluharty C.B., Fluharty A.L.;
RL "Structure of the asparagine-linked sugar chains of porcine kidney and
RX human urine cerebroside sulfate activator protein.";
RA J. Mass Spectrom. 35:1416-1424 (2000).
RA SAPOSIN D DISULFIDE BONDS.
RX MEDLINE=99337688; PubMed=10406958;
RA Tatti M., Salvio R., Ciaffoni P., Pucci P., Andolfo A.,
RT Amoresano A., Vaccaro A.M.;
RL "Structural and membrane-binding properties of saposin D.";
RX Query Match 100.0%; Score 412; DB 1; Length 524;
RT Best Local Similarity 100.0%; Pred. No. 2.6e-30;
RM Matches 80; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
QY 1 SDVYCEVCEFLVKEVTKLIDNNKTEKILDAFDKMCCKLPKSLSECCQEVVDVTGSSILS 60
DB |||||||
QY 61 ILLEEVSPFLVCSMLHLCSSG 80
DB |||||||
DB 371 ILLEEVSPFLVCSMLHLCSSG 390
RESULT 3
Q53FJ5 HUMAN
ID Q53FJ5_HUMAN PRELIMINARY; PRT; 524 AA.

AC Q53FJ5;
DT 13-SEP-2005 (TrEMBLrel. 31, Created)
DT 13-SEP-2005 (TrEMBLrel. 31, Last sequence update)
DT 13-SEP-2005 (TrEMBLrel. 31, Last annotation update)
DE Prosaposin (Variant Gaucher disease and variant metachromatic
DE leukodystrophy) variant (Fragment).
OS Homo sapiens (Human)
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini; Hominidae;
OC Homo.
OX NCBI_TaxID=9606;
RN [1]
RP NUCLEOTIDE SEQUENCE.
RC TISSUE=Synovial membrane;
RA Maruyama K., Sugano S.;
RT "Oligo-capping: a simple method to replace the cap structure of
RT eucaryotic mRNAs with oligoribonucleotides.";
RL Gene 138:171-174 (1994).
RN [2]
RP NUCLEOTIDE SEQUENCE.
RC TISSUE=Synovial membrane;
RA Suzuki Y., Yoshitomo K., Maruyama K., Sugano S.;
RT "Construction and characterization of a full length-enriched and a 5'-
RT end-enriched cDNA library.";
RL Gene 200:149-156 (1997).
RN [3]
RP NUCLEOTIDE SEQUENCE.
RC TISSUE=Synovial membrane;
RA Suzuki Y., Sugano S., Totoki Y., Toyoda A., Takeda T., Sakaki Y.,
RA Tanaka A., Yokoyama S.;
RL Submitted (Apr-2005) to the EMBL/GenBank/DBJ databases.
DR EMBL; AK223290; BAD97010.1; -, mRNA.
FT NON TER 1
SQ SEQUENCE 524 AA; 58140 MW; 7034F0C71C2226BC CRC64;
Query Match 100.0%; Score 412; DB 2; Length 524;
Best Local Similarity 100.0%; Pred. No. 2.6e-30;
Matches 80; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
QY 1 SDVYCEVCEFLVKEVTKLIDNNKTEKILDAFDKMCCKLPKSLSECCQEVVDVTGSSILS 60
DB |||||||
QY 61 ILLEEVSPFLVCSMLHLCSSG 80
DB |||||||
DB 371 ILLEEVSPFLVCSMLHLCSSG 390
RESULT 4
Q53FJ5 HUMAN
ID Q53FJ5_HUMAN PRELIMINARY; PRT; 524 AA.
AC Q53FJ5;
DT 10-MAY-2005 (TrEMBLrel. 30, Created)
DT 10-MAY-2005 (TrEMBLrel. 30, Last sequence update)
DT 13-SEP-2005 (TrEMBLrel. 31, Last annotation update)
DE Prosaposin (Variant Gaucher disease and variant metachromatic
DE leukodystrophy).
GN Name=PSAP; ORFNames=RP11-472K8.1-001;
OS Homo sapiens (Human)
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini; Hominidae;
OC Homo.
OX NCBI_TaxID=9606;
RN [1]
RP NUCLEOTIDE SEQUENCE.
RC TISSUE=Synovial membrane;
RA Heath P.;
RL Submitted (MAY-2005) to the EMBL/GenBank/DBJ databases.
RN [2]
RP NUCLEOTIDE SEQUENCE.
RA Kalline N., Chen X., Rolfs A., Halleck A., Hines L., Eisenstein S.,
RA Koundinya M., Raphael J., Moreira D., Kelley T., LaBaer J., Lin Y.,
RA Phelan M., Farmer A.;
RT "Cloning of human full-length cDNAs in BD Creator(TM) System Donor
RT

GenCore version 5.1.6
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OM protein - protein search, using sw model

Run on: January 13, 2006, 16:16:04 ; Search time 27.947 Seconds
(without alignments)
1257.748 Million cell updates/sec

Title: US-10-801-517-2

Perfect score: 412

Sequence: 1 SDVYCVCEFLVKEVTKLID.....ILLEVSPELVCSMLHLCSG 80

Scoring table: BLOSUM62

Gapop 10.0 , Gapext 0.5

Searched: 2443163 seqs, 439378781 residues

Total number of hits satisfying chosen parameters: 2443163

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%

Maximum Match 100%

Listing first 45 summaries

Database :

A_Geneseq_21:*

- 1: Geneseq19808:*
- 2: Geneseq19908:*
- 3: Geneseq20008:*
- 4: Geneseq20018:*
- 5: Geneseq20028:*
- 6: Geneseq20038:*
- 7: Geneseq20048:*
- 8: Geneseq20058:*
- 9: Geneseq20068:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match	Length	DB ID	Description
1	412	100.0	80	2 AAR70784	AAR70784 Saposin-C
2	412	100.0	80	2 AAR85653	AAR85653 Human sap
3	412	100.0	80	4 AAU05697	AAU05697 Human Sap
4	412	100.0	80	7 ABU62252	ABU62252 Shingoli
5	412	100.0	80	8 ADQ94329	ADQ94329 Human pro
6	412	100.0	80	8 ADU48631	ADU48631 Human Sap
7	412	100.0	80	8 ADW80728	ADW80728 Human sap
8	412	100.0	80	9 ADZ88479	ADZ88479 Human sap
9	412	100.0	210	6 ABU05201	ABU05201 Human exp
10	412	100.0	385	6 ABR41750	ABR41750 Human DIT
11	412	100.0	479	6 ABR39442	ABR39442 Human GEN
12	412	100.0	522	8 ADU24090	ADU24090 Human cys
13	412	100.0	523	4 AAB31916	AAB31916 Amino aci
14	412	100.0	523	6 ABU05211	ABU05211 Human exp
15	412	100.0	524	2 AAR70783	AAR70783 Prosaposi
16	412	100.0	524	2 AAR85652	AAR85652 Human pro
17	412	100.0	524	3 AAY58716	AAY58716 Human pro
18	412	100.0	524	6 ABU79099	ABU79099 Lip-TAA b
19	412	100.0	524	6 ABU05200	ABU05200 Human exp
20	412	100.0	524	6 ABU05207	ABU05207 Human exp
21	412	100.0	524	6 ABU05203	ABU05203 Human exp
22	412	100.0	524	6 ABU07340	ABU07340 Human exp
23	412	100.0	524	6 ABU05216	ABU05216 Human exp
24	412	100.0	524	6 ABU05202	ABU05202 Human exp

25	412	100.0	524	6 ABU05208	ABU05208 Human exp
26	412	100.0	524	6 ABU05214	ABU05214 Human exp
27	412	100.0	524	6 ABU05215	ABU05215 Human exp
28	412	100.0	524	6 ABU05199	ABU05199 Human exp
29	412	100.0	524	6 ABU05212	ABU05212 Human exp
30	412	100.0	524	6 ABU05213	ABU05213 Human exp
31	412	100.0	524	6 ABU05205	ABU05205 Human exp
32	412	100.0	524	7 ADF43340	ADf43340 Superant
33	412	100.0	524	7 ADJ69401	ADj69401 Human hea
34	412	100.0	524	8 ADO08060	ADo08060 Human pol
35	412	100.0	524	8 ADQ94328	ADq94328 Human Pre
36	412	100.0	524	8 ABM81149	ABm81149 Tumour-as
37	412	100.0	524	8 ADS87894	ADs87894 Human pro
38	412	100.0	524	8 ADU48630	ADU48630 Human pro
39	412	100.0	524	9 ADW80727	ADw80727 Human pro
40	412	100.0	524	9 ADX06774	ADx06774 Cyclin-de
41	412	100.0	524	9 ADY14302	ADy14302 PRO polypp
42	412	100.0	526	6 ABU05209	ABU05209 Human exp
43	412	100.0	527	4 AAB31915	AAB31915 Amino aci
44	412	100.0	527	5 ABP68602	ABp68602 Human pan
45	412	100.0	527	6 ABU79100	ABu79100 Lip-TAA b

ALIGNMENTS

RESULT 1

AAR70784 AAR70784 standard; protein; 80 AA.

AC AAR70784;

DT 25-MAR-2003 (revised)

DT 30-AUG-1995 (first entry)

XX Saposin-C.

XX Saposin-C; neuron; myelination; nervous system; neuroblastoma;
XX neurotrophic peptide; multiple sclerosis; leukoencephalitis;
XX adrenal leukodystrophy.

XX Homo sapiens.

XX WO9503821-A1.

XX 09-FEB-1995.

XX 28-JUL-1994; 94WO-US008453.

XX 30-JUL-1993; 93US-00100247.

XX 21-APR-1994; 94US-00232513.

XX (OBRI) O'BRIEN J S.

XX O'brien JS, Kishimoto Y;

XX WPI; 1995-082029/11.

XX Stimulating neural cell out-growth and myelination - with pro:saposin,
XX saposin C or new neurotrophic peptide(s) from cytokine(s), for treating
XX nervous system diseases.

XX Disclosure; Page 32; 50pp; English.

XX The peptide given in AAR70773, corresponding to amino acids 8-29 of human
XX saposin-C (AAR70784), promotes neurite outgrowth in vitro. A consensus
XX sequence was determined by comparing the peptide with hematopoietic and
XX neurotrophic cytokines, and neurotrophic peptides (AAR70774-82) were
XX identified in the AB loop of human ciliary neurotrophic factor,
XX interleukin-6, -2, -3 and -gamma, erythropoietin and leukocyte
XX inhibitory factor, and in helix C of human interleukin-1-beta and
XX oncostatin-M. Prosaposin (AAR70783) and saposin-C also promoted nerve
XX cell myelination ex vivo. (Updated on 25-MAR-2003 to correct PN field.)

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CC (Updated on 25-MAR-2003 to correct PA field.) (Updated on 25-MAR-2003 to
CC correct PI field.)
XX Sequence 80 AA;
SQ Query Match 100.0%; Score 412; DB 2; Length 80;
Best Local Similarity 100.0%; Pred. No. 2.4e-40;
Matches 80; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
QY 1 SDVYCEVCEFLVKEVTKLIDNNKTEKILDAFDMCKSLPKSLSECEQVVDVTGSSILS 60
DB 1 SDVYCEVCEFLVKEVTKLIDNNKTEKILDAFDMCKSLPKSLSECEQVVDVTGSSILS 60
QY 61 ILLEEVSPVLCSMLHLCSSG 80
DB 61 ILLEEVSPVLCSMLHLCSSG 80
RESULT 2
AAW85653
ID AAW85653 standard; peptide; 80 AA.
XX
AC AAW85653;
XX
DT 19-JUL-1999 (first entry)
XX
DE Human saposin C.
XX
KW Prosaposin; saposin; prosaptides; prosaposin receptor agonists; PRA;
KW peripheral nervous system; central nervous system; PNS; CNS; Akt; Bcl-2;
KW therapy; treatment; apoptosis; caspase; tumour necrosis factor; TNF;
KW cytokine; interferon gamma; IFN; inflammation; rheumatoid arthritis;
KW Crohn's disease; irritable bowel syndrome; asthma; cardiac infarction;
KW congestive heart failure; multiple sclerosis;
KW acute disseminated inflammatory leukoencephalitis;
KW progressive multifocal leukoencephalitis; Alzheimer's disease;
KW Parkinson's disease; amyotrophic lateral sclerosis; Huntington's disease;
KW ischemic heart disease; Guillain-Barre disease; alopecia; AIDS dementia;
KW cerebral malaria; HTLV; neuropathy;
KW inflammatory neurodegenerative disease; toxin-induced liver disease.
XX
OS Homo sapiens.
XX
XX WO9912559-A1.
XX
PD 18-MAR-1999.
XX
PF 09-SEP-1998; 98WO-US019216.
XX
PR 09-SEP-1997; 97US-0058352P.
PR 04-JUN-1998; 98US-0088129P.
XX
XX (REGC) UNIV CALIFORNIA.
XX
XX O'brien JS;
XX
XX WPI; 1999-229139/19.
XX
XX Use of prosaposin receptor agonist.
XX
XX Claim 7; Fig 2; 90pp; English.
XX
CC Prosaposin is a 70kDa glycoprotein which is proteolytically processed to
CC generate saposins A, B, C and D, all of which are similar to each other
CC and have a similar placement of six cysteines, a glycosylation site and
CC conserved proline residues. Prosaposin, saposin C and prosaposin derived
CC peptides (prosaptides), have therapeutic applications in promoting
CC recovery after toxic, traumatic, myocardial ischaemic, degenerative and
CC inherited lesions to the peripheral and central nervous system.
CC Prosaposin receptor agonists (PRA) inhibit proinflammatory cytokine-
CC induced apoptosis by activation of the Ser/thr protein kinase Akt. Akt
CC dissociates complexes of Bcl-2 family members, such as BAD-Bcl-2,
CC releasing Bcl-2 and its family members which inhibit caspases, thereby

CC inhibiting apoptosis. An additional mechanism whereby PRA's inhibit
CC apoptosis is by blocking activation of JNK, a proapoptotic signaling
CC component. Within several minutes after binding to the receptor, PRA's
CC block JNK activation induced by tumor necrosis factor-alpha (TNF alpha).
CC The activation of JNK by TNF alpha is another well known mechanism for
CC TNF alpha-induced, as well as other proinflammatory cytokine-induced
CC apoptosis. The method can be used for inhibiting apoptosis which is
CC caspase-mediated or induced by a proinflammatory cytokine, for example
CC TNF alpha or interferon-gamma. It can be used for inhibiting apoptosis
CC associated with a disorder such as e.g. rheumatoid arthritis, Crohn's
CC disease, irritable bowel syndrome, asthma, cardiac infarction, congestive
CC heart failure, multiple sclerosis, acute disseminated inflammatory
CC leukoencephalitis, progressive multifocal leukoencephalitis, Alzheimer's
CC disease, Parkinson's disease, amyotrophic lateral sclerosis, Huntington's
CC disease, ischemic heart disease, Guillain-Barre disease, traumatic brain
CC injury, traumatic spinal cord injury, alopecia, AIDS dementia, cerebral
CC malaria, HTLV, neuropathy, inflammatory neurodegenerative disease, and
CC toxin-induced liver disease. Saposin C acts as a prosaposin receptor
CC agonist
XX
SQ Sequence 80 AA;
Query Match 100.0%; Score 412; DB 2; Length 80;
Best Local Similarity 100.0%; Pred. No. 2.4e-40;
Matches 80; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
QY 1 SDVYCEVCEFLVKEVTKLIDNNKTEKILDAFDMCKSLPKSLSECEQVVDVTGSSILS 60
DB 1 SDVYCEVCEFLVKEVTKLIDNNKTEKILDAFDMCKSLPKSLSECEQVVDVTGSSILS 60
QY 61 ILLEEVSPVLCSMLHLCSSG 80
DB 61 ILLEEVSPVLCSMLHLCSSG 80
RESULT 3
AAU05697
ID AAU05697 standard; protein; 80 AA.
XX
AC AAU05697;
XX
DT 24-OCT-2001 (first entry)
XX
DE Human Saponin C, SapC.
XX
KW Human; glucocerebrosidase; GCB; lysosomal storage disease;
KW Gaucher's disease; Fabry's disease; Farber's disease;
KW G m l gangliosidosis; Tay-Sach's disease; Niemann-Pick disease;
KW Shindler disease; Hunter syndrome; Sly syndrome; Huler syndrome;
KW Scheie syndrome; Saponin C; SapC.
XX
OS Homo sapiens.
XX
XX WO200149830-A2.
XX
XX 12-JUL-2001.
XX
XX 29-DEC-2000; 2000WO-DK000743.
XX
XX 30-DEC-1999; 99DK-00001891.
XX 02-JUN-2000; 2000DK-00000865.
XX 02-JUN-2000; 2000DK-00000866.
XX 30-JUN-2000; 2000DK-00001027.
XX
XX (MAXY-) MAXYGEN APS.
XX
XX Okkels JS, Jensen AD, Halkier T, Jensen RB, Schambye HT;
XX WPI; 2001-465259/50.
XX
XX Improved lysosomal enzymes and lysosomal enzyme activators useful for
XX treating Gaucher's disease.
XX

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Example 5; Page 96; 97pp; English.

PS The sequence represents human Saponin C (SapC), an essential co-factor
XX for the lysosomal enzyme glucocerebrosidase, GCB. GCB is the enzyme
CC involved in Gaucher's disease, a lysosomal storage disease. The invention
CC relates to introducing new glycosylation sites into lysosomal
CC enzymes/activators like GCB to improve their bioactivity. The novel
CC polypeptides are used for the prevention and treatment of Gaucher's
CC disease, Fabry's disease, Farber's disease, G.m.1 gangliosidosis, Tay-
CC Sach's disease, Niemann-Pick disease, Shindler disease, Hunter syndrome,
CC Sly syndrome, Hurler and Hurler and Scheie syndromes

XX Sequence 80 AA;

Query Match 100.0%; Score 412; DB 4; Length 80;
Best Local Similarity 100.0%; Pred. No. 2.4e-40;
Matches 80; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 SDVYCEVCEFLVKEVTKLIDNNKTEKEILDADFDMCKSLPKSLSECEQVVDVTGSSILS 60
Db 1 SDVYCEVCEFLVKEVTKLIDNNKTEKEILDADFDMCKSLPKSLSECEQVVDVTGSSILS 60

QY 61 ILLEEVSPFLVCSMLHLCSSG 80
Db 61 ILLEEVSPFLVCSMLHLCSSG 80

RESULT 4

ABU62452
ID ABU62252 standard; protein; 80 AA.

XX AC ABU62252;

XX DT 29-AUG-2003 (first entry)
XX DE Sphingolipid activator protein C (saposin C).

XX Sphingolipid activator protein; saposin; neuroprotective; human;

XX KW Gene therapy; anionic phospholipid; fusogenic protein; prosaposin;
XX KW Gaucher's disease; saposin C.

XX OS Homo sapiens.

XX PN US2003095999-A1.

XX PD 22-MAY-2003.

XX PF 09-FEB-2001; 2001US-00780438.

XX PR 11-FEB-2000; 2000US-0181754P.

XX PA (QIIX/) QI X.

XX PI QI X;

XX PS WPI; 2003-512933/48.

XX PT Delivering pharmaceutical agent through membrane used for treating
XX PT Gaucher's disease, by applying composition comprising anionic
XX PT phospholipids and fusogenic protein derived from prosaposin in carrier to
XX PT membrane.

XX Disclosure; Fig 4; 19pp; English.

XX The invention describes a method of delivering a pharmaceutical agent
XX through a membrane comprising applying to the membrane a composition (1)
XX comprising: (1) anionic phospholipids; (2) a pharmaceutical agent
XX contained within the phospholipids, and (3) a fusogenic protein or
XX polypeptide derived from prosaposin in a carrier. The method can be used
XX for delivering pharmaceutical agents through a biological membrane in
XX cosmetic and medicinal applications, particularly for treating Gaucher's
XX disease. This is the amino acid sequence of sphingolipid activator
XX protein C (saposin C) for use in the delivery composition

XX Sequence 80 AA;

Query Match 100.0%; Score 412; DB 7; Length 80;
Best Local Similarity 100.0%; Pred. No. 2.4e-40;
Matches 80; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 SDVYCEVCEFLVKEVTKLIDNNKTEKEILDADFDMCKSLPKSLSECEQVVDVTGSSILS 60
Db 1 SDVYCEVCEFLVKEVTKLIDNNKTEKEILDADFDMCKSLPKSLSECEQVVDVTGSSILS 60

QY 61 ILLEEVSPFLVCSMLHLCSSG 80
Db 61 ILLEEVSPFLVCSMLHLCSSG 80

RESULT 5

ADQ94329
ID ADQ94329 standard; protein; 80 AA.

XX AC ADQ94329;

XX DT 23-SEP-2004 (first entry)

XX DE Human Prosaposin protein, C-domain.

XX KW Human; prosaposin; C-domain; prosaposin receptor agonist;

XX KW neuropathic pain; neurite outgrowth; neural cell death; myelination;

XX KW demyelination; neuropathy; peripheral nerve disorder; neuroma;

XX KW nerve compression; nerve crush; nerve stretch;

XX KW incomplete nerve transection; mononeuropathy; polyneuropathy.

XX OS Homo sapiens.

XX PN US2004121958-A1.

XX PD 24-JUN-2004.

XX PF 24-DEC-2003; 2003US-00746442.

XX PR 05-MAR-1996; 96US-00611307.

XX PR 05-MAR-1997; 97WO-0004143.

XX PR 11-SEP-1997; 97US-00928074.

XX PA (REGC) UNIV CALIFORNIA.

XX PI O'brien JS;

XX PS WPI; 2004-468194/44.

XX PT New prosaposin receptor agonist, useful in alleviating or treating
XX PT neuropathic pain, inhibiting the onset of neuropathic pain, neural cell
XX PT death, demyelination, or sensory or motor neuropathy, and stimulating
XX PT neurite outgrowth.

XX Disclosure; SEQ ID NO 24; 33pp; English.

XX The invention relates to a prosaposin receptor agonist comprising a
XX defined amino acid sequence of 14-50 amino acids conforming to the
XX consensus sequence appearing as ADQ94330. The agonists are based on
XX peptides derived from the C domain of human prosaposin (or homologous
XX peptides from other proteins). Also included are a pharmaceutical
XX composition comprising the prosaposin receptor agonist in a
XX pharmaceutical carrier, a method of alleviating neuropathic pain in a
XX subject, a method of inhibiting the onset of neuropathic pain in a
XX subject, a method of stimulating neurite outgrowth (or inhibiting neural
XX cell death, promoting myelination or inhibiting demyelination) and a
XX method of inhibiting sensory or motor neuropathy. The neuropathic pain
XX results from a peripheral nerve disorder, e.g. neuroma, nerve
XX compression, nerve crush, nerve stretch and incomplete nerve
XX transection, mononeuropathy or polyneuropathy or results from a disorder
XX of dorsal root ganglia, spinal cord, brainstem, thalamus, or cortex. The
XX prosaposin receptor agonist, composition, and methods are useful in

Matches 80; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
QY 1 SDVYCEVCEFLVKEVTKLIDNNKTEKILDAFDKMCCKLPSLSECEQVVDYTGSSILS 60
DB 1 SDVYCEVCEFLVKEVTKLIDNNKTEKILDAFDKMCCKLPSLSECEQVVDYTGSSILS 60
QY 61 ILLEEVSPRLVCSMLHLCSSG 80
DB 61 ILLEEVSPRLVCSMLHLCSSG 80

RESULT 8
AD288479
ID AD288479 standard; protein; 80 AA.
AC AD288479;
XX
DT 14-JUL-2005 (first entry)
XX
DE Human saposin C fusogenic protein.
XX
KW Saposin C; pharmaceutical; drug delivery; cosmetics; gauchers disease;
KW metabolic; neurological disease; beta-glucosidase activator;
KW sphingolipid activator protein.
OS Homo sapiens.

Key Location/Qualifiers
FT Binding-site 3..15
FT Region /note= "Lipid binding region"
FT Region 4..19
FT Disulfide-bond /note= "Helix 1"
FT Disulfide-bond 5..78
FT Disulfide-bond 8..72
FT Region 17..33
FT Region /note= "Neuritogenic region"
FT Region 25..40
FT Disulfide-bond /note= "Helix 2"
FT Region 43..61
FT Active-site /note= "Helix 3"
FT Region /note= "Beta-glucosidase activation region"
FT Binding-site /note= "Helix 4"
FT Binding-site 65..76
FT Binding-site /note= "Lipid binding region"

US2005100591-A1. (10/967,921)
12-MAY-2005.
18-OCT-2004; 2004US-00967921.
PR 11-FEB-2000; 2000US-0181754P.
PR 09-FEB-2001; 2001US-00780438.
XX (Q1XX/) Q1 X.
XX Q1 X;
XX
XX WPI, 2005-345361/35.
XX
XX Delivering a pharmaceutical agent through a dermal or mucosal membrane to
XX e.g. treat Gaucher's disease, comprises applying to the membrane a
XX composition comprising a fusogenic protein, such as saposin C.
XX
XX Disclosure; Fig 4; 26pp; English.
XX
XX The present invention relates to methods of delivering pharmaceutical
XX agents across biological membranes where the pharmaceutical agent is
XX contained within the phospholipid membrane and delivery is facilitated by
XX a membrane fusogenic protein, saposin, derived from prosaposin. Saposins

CC are sphingolipid activator proteins or coenzymes that also promotes acid
CC beta-glucosidase activity by inducing the enzyme conformational change at
CC acidic pH. The methods and composition of the invention are useful for
CC enhancing the transport and delivery of pharmaceutical agents across
CC and/or within dermal and mucosal membranes for both cosmetic and
CC medicinal applications such as in treating Gaucher's disease. The present
CC sequence is human saposin C fusogenic protein.
XX
SQ Sequence 80 AA;

Query Match 100.0%; Score 412; DB 9; Length 80;
Best Local Similarity 100.0%; Pred. No. 2.4e-40;
Matches 80; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
QY 1 SDVYCEVCEFLVKEVTKLIDNNKTEKILDAFDKMCCKLPSLSECEQVVDYTGSSILS 60
DB 1 SDVYCEVCEFLVKEVTKLIDNNKTEKILDAFDKMCCKLPSLSECEQVVDYTGSSILS 60
QY 61 ILLEEVSPRLVCSMLHLCSSG 80
DB 61 ILLEEVSPRLVCSMLHLCSSG 80

RESULT 9
ABU05201
ID ABU05201 standard; protein; 210 AA.
XX
AC ABU05201;
XX
DT 29-JAN-2003 (first entry)
XX
DE Human expressed protein tag (EPT) #1867.
XX
KW Translational profiling; expressed protein tag; EPT; kinase; phosphatase;
KW protease; protease inhibitor; transporter; cytoskeletal protein;
KW receptor; transcription factor; cancer; MHC;
KW major histocompatibility complex; myeloma; colon cancer; gastric cancer;
KW adenocarcinoma; sarcoma; melanoma; lymphoma; leukaemia.
OS Homo sapiens.
XX
XX WO200278524-A2.
XX
XX 10-OCT-2002.
XX
XX 28-MAR-2002; 2002WO-US009671.
XX
XX 28-MAR-2001; 2001US-0279495P.
XX 21-MAY-2001; 2001US-0292544P.
XX 08-AUG-2001; 2001US-0310801P.
XX 01-OCT-2001; 2001US-0326370P.
XX 04-DEC-2001; 2001US-0336780P.
XX 20-FEB-2002; 2002US-0358985P.
XX (ZYCO-) ZYCO INC.
XX
XX Chicx RM, Tomlinson AJ, Urban RG;
XX WPI, 2003-040607/03.
XX
XX New polypeptides (e.g. kinases, phosphatases, proteases, transporters,
XX cytoskeletal proteins, receptors or transcription factors), useful for
XX treating cancer, e.g. colon cancer, gastric cancer, sarcoma, lymphoma or
XX leukemia.

Example 2; SEQ ID NO 1867; 134pp; English.
XX
XX The invention describes a purified polypeptide, which comprises a
XX fragment of a kinase, phosphatase, protease, protease inhibitor,
XX transporter, cytoskeletal protein, receptor or transcription factor. The
XX polypeptide is useful as an immunogenic composition for eliciting in a
XX mammal an immunogenic response directed against any of the purified
XX polypeptide. The purified polypeptide, or the antibody that binds to this